

REMARKS

Claims 8-13, 16, 19, 20, 22-24, 26 and 71-93 are pending. No new matter has been added.

Priority Under 35 USC §119

Applicants gratefully acknowledge the Office statement on pg. 2 of the Action, paragraph 3, that they are entitled to a priority date of September 15, 2001 for claims supported by PCT/KR02/01728 (WO 03/025226). Applicants submit that at least pending claims 8-13, 19, 20, 22-24, 26, 71-83, and 87-93 are entitled to that priority date. In particular, see claims 1-14 of the '226 PCT application as well as Figs. 1, 3A, and 3B as well as supporting disclosure under "Disclosure of the Invention", pgs. 8-16 and the Examples section of the PCT application for support. See also at page 13, lines 20-21 (claim 20), page 13, lines 20-21 and page 14, lines 7-8 (claim 24). Claims 71 and 72 are also supported, for instance, by claims 9, 10 and 12 of the PCT application. Support for claim 82 can also be found at page 17, lines 20-21 of the PCT application. Support for claim 89 can be found in Figures 3A and 3B of the PCT application. Support for claim 90, particularly as amended, can also be found in Figures 3A and 3B (showing, among other things, a wall (3 mm) between the sample and the heat sources).

Additional basis for Applicants' priority claim has been set forth in the Response To Final Office Action dated 31 October 2007 submitted with the RCE.

Accordingly, Applicants respectfully submit that they are entitled to a priority date of September 15, 2001 (or earlier) for at least pending claims 8-13, 19, 20, 22-24, 26, 71-83, and 87-93 of the instant application since at least these claims are supported by the PCT/KR02/01728 application as filed.

Double Patenting Rejection

The Office provisionally rejected claims 8, 16 and 20 on the ground of obviousness-type double patenting as being unpatentable over claims 7 and 8 of co-pending application no. 10/836,376. As the rejection is provisional, Applicants will address the rejection if patent

application Ser. No. 10/836,36 is granted prior to the instant application and the claims of the instant application are otherwise in condition for allowance.

Claim Rejections Under 35 USC § 103

Claims 8-12, 19-20, 22-23, and 26 stand rejected as being unpatentable over Hunicke-Smith WO 97/48818 in view of Benett et al. WO 02/072267 (hereinafter «Benett») and further in view of Haff et al. US Pat. No. 5,720,923. Applicants respectfully traverse the rejection on grounds that the Office has not established a *prima facie* case.

In particular, the Office alleged that Benett had a US priority date of March 9, 2001. Office Action at pg. 6. Applicants respectfully disagree on grounds that Benett should not qualify as prior art as of that date. For instance, it fails to designate the United States as a national stage entry country as specifically required by MPEP 706.02(f) (1), for example. Accordingly, the earliest prior art date of which Benett can be used by the Office is the international publication date of 19 September 2002. However, that date is well after the priority date of the instant application. Accordingly, Benett as relied on is not prior art as to the instant application since it cannot be used as of its US priority date. MPEP 706.02 (f)(1) .

In view thereof, the Office has not made a *prima facie* case of obviousness and the rejection should be withdrawn.

Declaration Under 37 CFR 1. 131

Applicants further traverse the rejection of claims 8-12, 19-20, 22-23 and 26 as set forth above on grounds that they conceived and reduced the claimed invention to practice well before 9 March 2001 ie., the US priority date alleged by the Office.

In particular, the attached Rule 131 Declaration provides evidence that the inventors conceived and reduced the claimed invention to practice well before that date. Accordingly, withdrawal of Benett as a reference on a further ground is respectfully requested.

Turning to the attached Rule 131 Declaration, the inventors state that they conceived and reduced the claimed invention to practice in the Republic of Korea («Korea») well before March 9, 2001. Decl. at ¶3. Korea became a WTO member country after January 1, 1996 and thus

inventive activities occurring after that date, as set forth in the Declaration for instance, can be used as a basis for establishing prior conception and reduction to practice of the claimed invention. 37 CFR 1.131, MPEP §§ 715 and 201.13.

In particular, it is stated at ¶4 of the Declaration that well before March 9, 2001 there was recognition by at least one inventor of the need to make a nucleic acid sequence amplification apparatus as described in the instant (subject) application that uses convection-based PCR (hereinafter «apparatus»). That conception included recognition of a need to make the apparatus with a plurality of heat sources which supply heat to or remove heat from a plurality of specific regions in a sample. See pending claims 8, 91 and 93 for instance.

It is further stated at ¶¶ 6-7 of the Declaration, that at least one inventor saw the need to make the apparatus well before March 9, 2001 in which the plurality of heat sources are arranged such that a first heat source that provides heat to a lower portion of the sample is located lower in height than a second heat source that removes heat from an upper portion of the sample. Further stated is recognition of need to configure the first heat source to create a spatial temperature distribution with spatial regions fulfilling temperature conditions suitable for convection PCR in the apparatus. See pending claims 8, 91 and 93 for instance.

As stated at ¶¶6-9 of the Declaration, there was recognition well before March 9, 2001 of particular convection PCR design parameters and amplification protocols for testing the apparatus.

As stated at ¶9 of the Declaration, at least one of the inventors made (or had made under their direction and supervision) a working example of the apparatus described in the subject application well before March 9, 2001. In particular, the Declaration provides a photograph (Appendix 2) showing various features of the apparatus including a first and second heat source and an insulator positioned between the first and second heat sources. See pending claims 8, 23, and 91, for instance. See also ¶17 of the Declaration which provides another photograph of the apparatus.

It is stated at ¶9 of the Declaration, that at least one of the inventors recognized the need to vary the depth of the sample hole in the first heat source to help optimize convection PCR

conditions within the apparatus. At least one of the inventors concluded well before March 9, 2001 that amplification using convection PCR could occur within the apparatus using a particular reaction volume and sample hole depth in the first heat source. See ¶21 of the Declaration.

It is stated at ¶¶10-11 of the Declaration that the apparatus was designed to have copper inlet and outlet tubes to accommodate a liquid (water) for thermal contact with a specific region of the sample in contact with the second heat source. As further stated, the second heat source was further designed well before March 9, 2001 to include a receptor in which the liquid was contained to remove heat from the sample. As further stated at ¶11 of the Declaration, the inlet and outlet tubes and the receptor of the second heat source were made to produce or assist a circulation unit that would circulate liquid through the apparatus. See pending claims 10 and 11, for example.

It is further stated at ¶12 of the Declaration that well before March 9, 2001 at least one inventor had made the apparatus to include a plurality of heat sources with a first thermally conductive solid in thermal contact with a lower portion of the sample and a second thermally conductive solid in thermal contact with an upper portion of the sample. As stated, copper was used to facilitate the heat transfer in the solids. See pending claim 19, for instance.

It is further stated at ¶13 of the Declaration that well before March 9, 2001 at least one of the inventors conceived and made the apparatus in which at least one of the heat sources included a thermally conductive solid in thermal contact with a specific region of the sample. See claim 9.

It is further stated at ¶14 of the Declaration that well before March 9, 2001, the apparatus was made to include an opening defined by the first and second heat sources and the insulator. See pending claim 73, for instance.

Particular opening configurations in the second heat source were made well before March 9, 2001 as stated at ¶15 of the Declaration. These included an opening for receiving the reaction vessels that included a first through hole within the second heat source, a second through hole within the insulator and an opening within the first heat source. See pending claims 75-78. As

stated at ¶16 of the Declaration, the apparatus was made to have certain sample through holes with a closed bottom end within the first heat source. See pending claims 74 and 92, for example.

As stated at ¶¶18-21 of the Declaration, at least one of the inventors identified and used reaction parameters to test the apparatus under convection PCR conditions well before March 9, 2001. In particular, the inventor had successfully demonstrated that the apparatus worked to amplify a nucleic acid sequence using convection PCR well before March 9, 2001. See ¶20 of the Declaration.

As stated at ¶¶ 22-26 of the Declaration, at least one of the inventors had detected and quantified a spatial temperature distribution within the apparatus when in use and well before March 9, 2001. In particular, at least one of the inventors had characterized a spatial temperature distribution with spatial regions fulfilling temperature conditions suitable for (i) a denaturation, (ii) an annealing step in which the single strand DNAs formed in the denaturation step hybridize to the primers to form DNA-primer complexes, and (iii) a polymerization step in which the primers in the DNA-primer complexes are extended by the polymerization reaction. See claims 8, 91 and 93 for instance.

As further stated at ¶27 of the Declaration, at least one of the inventors concluded before March 9, 2001 that the apparatus could produce a spatial temperature distribution that induces circulation of the sample by thermal convection so that the denaturation, annealing and polymerization steps could occur sequentially and repeatedly inside the sample. See claims 8, 91 and 93 for instance.

At least one of the inventors further concluded that the heat sources of the apparatus were arranged in the device to provide for the spatial temperature distribution had a convection region position between a relatively high temperature region (from the first heat source) and a relatively low temperature region (from the second heat source). See Decl. at ¶28 and pending claim 26, for instance.

As further stated at ¶¶29-32 of the Declaration, at least one of the inventors had conceived of and reduced to practice various reaction vessel configurations for use with the apparatus well before March 9, 2001. See pending claims 79-81, 83, and 87-88.

As also stated in the Declaration at ¶30, the inventors concluded from information that a reaction vessel with a single passage used in our apparatus achieved nucleic acid amplification through bidirectional convection (i.e., both upward and downward convection) within the reaction vessel. See claim 22.

It is also stated at ¶33 of the Declaration that well before March 9, 2001 at least one of the inventors conceived of the need to introduce a vertical gap between the top of the relatively high temperature region and the bottom of the relatively low temperature region, and also a gap between the sample and at least the second heat source. See claim 23, 24, 89 and 90.

The apparatus cited in the Rule 131 Declaration is disclosed throughout the subject application including the Drawings and claims as filed originally. For example, see Figs. 1, 3a, 3b (disclosing, for example, an example of the claimed invention and a reaction tube showing convection PCR). See also supporting disclosure under the Brief Description of the Drawings and under the «Best Mode For Carrying out the Invention» section of the instant application. See also the Examples section (providing particular reaction vessel configurations and conditions for performing convection PCR with the apparatus).

In view thereof, Applicants submit that they have provided sufficient evidence to show that the claimed invention was conceived and reduced to practice well before March 9, 2001. Since the present application claims priority to a date or dates less than one year after March 9, 2001, removal of Benett as a prior art reference is requested.

As relied on, none of the other references of record, taken individually or together, at enough to substantiate the instant obviousness rejection. Reconsideration and withdrawal of the rejection are therefore requested.

Remaining Rejections Under 35 USC § 103

Each of the remaining obviousness rejections in the present office action rely on Benett as cited by the Office. See paragraphs 11-16. Applicants respectfully submit that they have successfully antedated Benett as a prior art reference under 37 CFR 1.131. Accordingly, reconsideration and withdrawal of the remaining rejections are requested.

As relied on, none of the other references of record, taken individually or together, at enough to substantiate the instant obviousness rejection. Reconsideration and withdrawal of the rejection are therefore requested.

Conclusion

Applicants believe that no further fee is due to consider the present amendment. Nevertheless, the Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. **502486**.

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Respectfully submitted,

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